Response to Office Action Mailed January 23, 2008

A. Claims In The Case

Claims 1, 5-9, 11-14, 16-27, 29-32, and 63 have been rejected. Claims 11, 13, 14, 16-18, and 63 have been amended. Claims 24-31 have been canceled. Claims 1, 5-9, 11-14, 16-23, 32, and 63 are pending in the case.

B. The Claims Meet The Written Description Requirement

The Office Action rejected claims 24-31 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Applicant respectfully disagrees with this rejection, however, to expedite prosecution, Applicant has canceled claims 24-31.

C. The Claims Are Not Indefinite Pursuant To 35 U.S.C. § 112, Second Paragraph

Claims 11, 13-18, and 24-31 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully disagrees with this rejection, however, to expedite prosecution, Applicant has canceled claims 34-31 and amended claims 11 and 13-18 for clarification.

D. The Claims Are Not Obvious Over The Cited Art Pursuant To 35 U.S.C. § 103(a)

Claims 1-19, 21, 23, 25, 27, 29, 30, 32, 63 and 128 stand rejected under to 35 U.S.C. §103(a) as being obvious over the teachings of U.S. Patent No. 4,927,676 to Williams et al.

("Williams") in view of U.S. Patent No. 6,582,391 to Mineau-Hanschke ("Mineau '391") and U.S. Patent No. 6,419,920 to Mineau-Hanschke ("Mineau '920"), and if necessary in view of U.S. Patent No. 5,034,265 to Hoffman et al. ("Hoffman '265") or U.S. Patent No. 6,033,582 to Lee et al. ("Lee") or U.S. Patent No. 5,055,316 to Hoffman et al. ("Hoffman '316").

Claims 1 and 32 include, but are not limited to, the feature of:

> subjecting a bioresorbable polymeric substrate to a gas-plasma treatment, wherein subjecting the substrate to a gas-plasma treatment comprises exposing the substrate to a reactive gas, wherein the reactive gas comprises oxygen, and wherein the supplied energy during the gas-plasma treatment is between about 5 kJ and about 10 kJ.

In order to reject a claim as obvious, the Examiner has the burden of establishing a *prima facie* case of obviousness. *In re Warner et al.,* 379 F.2d 1011, 154 USPQ 173, 177-178 (CCPA 1967). To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974), MPEP § 2143.03.

With respect to the use of a gas plasma, the Office Action refers to Williams as "attaching endothelial cells to a substrate by treating the substrate with a gas-plasma. The Office Action further states that the references to Hoffman and Lee also cite gas plasma treatment conditions. Applicant submits, however, that none of these references teach or suggest a gas plasma treatment process in which the "supplied energy during the gas-plasma treatment is between about 5 kJ and about 10 kJ." As has been noted in Applicant's previous response, Applicant has determined that, unexpectedly, the supplied energy used during a plasma treatment has a significant effect on the formation of radical groups on the surface of the substrate. For example, Applicant's specification states:

> Gas-plasma treatment may induce formation of free radicals on a substrate. In an embodiment, gas-plasma treatment with a reactive gas that includes oxygen may induce formation of oxide free radicals on a substrate. As shown below, parameters chosen for a gas-plasma treatment may influence relative density of free radicals formed on the substrate.
>
> Data from the untreated substrate in Table 1 suggest that C=O, C-O, and C-C bonds are present in approximately equal numbers, with each bond type corresponding to approximately one-third of the carbon-containing surface bonds. Data from Table 2 for a substrate treated at a RF power of 100 watts for 1 minute suggest that gas-plasma treatment induced the formation of oxide radicals, with relative occurrences of C=O, C-O, C-C, and C-O-O bonds measured as 31.47%, 34.59%, 30.45%, and 3.49%, respectively. Data from Table 3 for a substrate treated at a RF power of 40 watts for 3 minutes suggest that gas-plasma treatment induced an even greater formation of oxide radicals, with relative occurrences of C=O, C-O, C-C, and C-O-O bonds measured as 39.12%, 31.77%, 22.70%, and 6.41%, respectively. Thus, the relative percentage of oxide radicals is almost twice as high for a 40 watt, 3 minute gas-plasma treatment than for a 100 watt, 1 minute gas-plasma treatment. Data from Table 4, with relative occurrences of C=O, C-O, and C-C bonds measured as 31.47%, 34.59%, and 30.45%, respectively, suggest that treatment at a RF power of 100 watts for 3 minutes does not promote formation of oxide radicals.
> (Specification, pg. 10, line 1 – pg. 11, line 17)

The formation of radicals on the surface of an implant is known to have a number of beneficial effects. For example, free radicals on implant surfaces may simulate in vivo vascular injury, thereby promoting endothelial cell activation and induction of blood vessel formation, or angiogenesis. Applicant has shown that bioresorbable polymeric substrates exposed to a reactive gas, wherein the reactive gas comprises oxygen, and wherein the supplied energy during the gas-plasma treatment is between about 5 kJ and about 10 kJ creates substrates having the unexpected benefit of additional radical formation on the surface. In addition, Applicant has shown that at supplied energies significantly above this range (for example, as shown in Table 4), little or no radical formation is seen. Thus Applicant has shown that the range of between 5 kJ and about 10 kJ exhibits a criticality that is not know in the prior art.

Applicant has shown the criticality of the claimed range of 5 kJ to about 10 kJ. In the experiment recited above, Applicant has shown that at a supplied energy of 6 kJ (See Specification, Table 2, paragraph [0038]) a significant amount of oxide radicals are produced. When the supplied energy is increased to 7.2 kJ (See Specification, Table 3, paragraph [0039]) the amount of oxide radicals produced increases, even though a lower power level is used. When the supplied energy is increased to 18 kJ, however, no oxide radicals appear to be formed (See Specification, Table 4, paragraph [0040]). Thus keeping the supplied energy within the claimed range of 5 kJ to about 10 kJ is a feature that is critical and not recognized in the prior art, especially given the large range of supplied energy taught by the prior art.

With respect to this feature the Office Action states:

> Williams et al. disclose plasma treatment conditions that provide an energy range that encompasses the claimed energy range, and selecting preferred optimum conditions within the range of conditions suggested by Williams et al. to provide the claimed energy range would have required merely limited routine experimentation and been obvious.
> (Office Action, page 8)

Applicant respectfully disagrees. With regard to the obviousness of ranges the MPEP states:

> [A] prior art reference that discloses a range encompassing a somewhat narrower claimed range is sufficient to establish a prima facie case of obviousness. ... However, if the reference's disclosed range is so broad as to encompass a very large number of possible distinct compositions, this might present a situation analogous to the obviousness of a species when the prior art broadly discloses a genus.
> (MPEP, Rev. 6, Sept. 2007, 2144.05(I))

With respect to supplied energy, Williams teaches:

> Ranges for these parameters which provide advantageous results are measured DC or AC power density levels of from 0.001 to 400 watts per cubic centimeter, oscillation frequencies up to 100 megahertz, 2 seconds to 12 hours, 0° to 200°C, and 0.01 to 100 torr. Preferred ranges for these parameters are 0.01 to 200 watts per cubic centimeter, 5 to 30 megahertz, 5 seconds to 120 minutes, 10°-50°C, and 0.01 to 20 torr.

The supplied energy (joules) is equal to power (watts) X time (seconds). Based on this relationship, Williams teaches a supplied energy ranging from 2×10^{-6} kJ to 17,280 kJ and, in preferred embodiments, Williams teaches a supplied energy range of from 5×10^{-5} kJ to 1440 kJ. Applicant submits that the range of Williams is so broad as to encompass a very large number of possibilities. Thus the use of a range of between about 5 kJ and about 10 kJ would not be obvious in view of such a large range, especially given the unexpected results obtained by the use of a supplied energy in Applicant's claimed range.

It is known that "Applicants can rebut a *prima facie* case of obviousness based on overlapping ranges by showing the criticality of the claimed range." (See MPEP, Rev. 6, Sept. 2007, 2144.05(III))

With regard to the selection of Applicant's claimed range being within routine experimentation of one skilled in the art, Applicant notes that "a particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation." (MPEP Rev. 6, Sept. 2007, 2144.05(II)(B)). The variable of "supplied energy" is not recognized in any of the prior art references as a "result-effective variable." While the cited references suggest various power levels and times of treatment, none of the prior art references teaches or suggests that the "supplied energy" is a variable that is controlled to produce a "result." None of the prior art references appear to have recognized that radical formation may be controlled by the supplied energy.

For at least these reasons, Applicant submits that the Applicant feature where the "supplied energy during the gas-plasma treatment is between about 5 kJ and about 10 kJ" in combination with the other features of Applicant's claims, is not obvious in view of the broadly recited ranges of the prior art, since the criticality of the supplied energy was not recognized.

With regard to Lee, Applicant notes that Lee appears to teach subjecting the substrate to a gas-plasma treatment that includes exposing the substrate to a reactive gas, wherein the reactive gas comprises oxygen. For example, Lee teaches that

> Poly(L-lactid acid) [PLLA], poly(glycolic acid) [PLGA], and poly (lactide-co-glycolide)[PLGA] PLLA, PGA, and PLGA are biodegradable polymers that can be etched with a noble gas RF plasma and water vapor at temperatures from about 25°C to about 50°C with chamber pressures preferably between about 0.1 Torr and about 1 Torr. When etching these polymeric materials, RF power levels should be between about 10 and about 200 watts; preferably between about 50 and about 150 watts.
> (Lee, Col. 13, lines 10-18)
>
> In the circumstances where guidance is required in determining etch time and/or reaction rate, an initial etch of 5-30 minutes may be tried.
> (Lee, Col. 8, line 67 – Col. 9, line 2)

Thus Lee teaches a supplied energy range from 3 kJ to 360 kJ.

Furthermore, Lee teaches the specific use of an oxygen containing plasma on a bioresorbable polymer, but at supplied energy that is higher than 10 kJ. Specifically, Lee states:

> For this example, poly(L-lactic acid) [PLLA] suture material (0.05 mm diameter) was subjected to a helium and an argon plasma with a small amount of water vapor. PLLA suture material was placed in a plasma reaction chamber with approximately 15-mL reservoir of distilled water to generate the reactive species. The chamber was evacuated to $5x10^{-5}$ Torr, Ar was introduced at a flow rate of approximately 50 sccm, and a chamber pressure of 0.050 Torr was established.

> The RF power source was switched to the power mode and set to 80 watts. Reactive etching continued for a total of 75 minutes at an operating temperature of approximately 25° C. (room temperature), at which point the power was turned off and the chamber was evacuated to 5×10^{-6} Torr. The chamber was allowed to equilibrate to standard atmospheric conditions and the etched PLLA material was removed and was subsequently examined with SEM. In a second experiment, identical procedures are employed to etch a second sample of PLLA suture material except that helium (He) is used in the plasma rather than Ar.
> (Lee, Col. 21, line 66 – Col. 2, line 17)

Lee appears to teach that the treatment of PLLA is performed using a power setting of 80 watts for a time of 75 minutes. This would represent a supplied energy of:

80 watts X 4500 seconds = 360,000 J (36 kJ)

Such an energy is significantly greater than Applicant's claimed upper range of 10 kJ. As noted above, treatment at supplied energies above 10kJ significantly reduces the amount of radicals formed on the surface and reduces the effectiveness of an implant made at the higher energies. (For example, as noted above, a supplied energy of 18 kJ did not produce any significant oxide radical formation.) Thus, for at least the same reasons cited above for Williams, Applicant submits that it would not be obvious to control the supplied energy to be in the range of between about 5 kJ to about 10 kJ.

For at least these reasons, Applicant submits that independent claims 1, 32, and 63 are patentable over the combination of references cited.

C. Summary

Based on the above, Applicant submits that all claims are now in condition for allowance. Favorable reconsideration is respectfully requested.

Applicant respectfully requests a three-month extension of time to respond to the Office Action dated January 23, 2009. A fee authorization is enclosed for the extension of time fee. If any further extension of time is required, Applicant hereby requests the appropriate extension of time. If any fees are inadvertently omitted or if any additional fees are required or have been overpaid, please appropriately charge or credit those fees to Meyertons, Hood, Kivlin, Kowert & Goetzel, P.C. Deposit Account Number 50-1505/5660-00503/EBM

Respectfully submitted,

/Eric B. Meyertons/

Eric B. Meyertons
Reg. No. 34, 876

Attorney for Applicant

MEYERTONS, HOOD, KIVLIN, KOWERT & GOETZEL, P.C.
P.O. BOX 398
AUSTIN, TX 78767-0398
(512) 853-8800 (voice)
(512) 853-8801 (facsimile)

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